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International Application No.	PCT/US04/037813
International Filing Date:	12 November 2004
Applicant:	University of South Carolina et al.
Priority Date:	12 November 2003
Agents File Reference:	16139/09052
Authorized Officer:	David Bouveret

TO: The International Bureau of WIPO
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1211 Geneva 20,
Switzerland

LETTER

Dear Madam or Sir:

The Applicant wishes to amend the claims of this application under the terms of Art 19 PCT. Although no International Search Report has yet been received for the present application, Applicant wished to file its amendments prior to the expiration of the statutory time period for Chapter I prosecution. Accordingly, it is respectfully requested that this amendment be entered into the case at an appropriate time under the terms of Art 19 PCT.

Amendment of the claims:

Please amend the claims by adding new claims 44 and 45. Claim 44 depends from claim 1 and claim 45 depends from claim 44. It is believed, therefore, that neither claim introduces a new issue regarding unity of invention.

New claim 44 further describes a method of preventing or treating a cardiovascular or respiratory disorder in a subject by administering an effective amount of a compound of claim 1 in combination with a conventional treatment agent. Claim 45

describes the conventional treatment agent as a calcium channel blocker. Support for these features is found in the original specification at least at the following locations:

Paragraph 105 teaches that a combination therapy of a compound described by formula I herein and conventional treatment agent may also be useful for decreasing the required number of separate dosages, thus, potentially improving patient compliance. This shows that the formula I compound can be used with a separate conventional treatment agent.

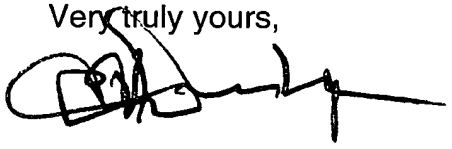
Paragraph 100 teaches that "[a]s used herein, the terms "conventional treatment agent" or conventional treatment agents" refer to any compound that is other than a compound described according to formula I and is either already known or is later discovered to have efficacy for the prevention and/or treatment of a cardiovascular and/or a respiratory disorder." And paragraph 10 teaches that, "[c]urrently, vasodilators, together with CCBs [calcium channel blockers] and angiotensin inhibitors, are the accepted choice as first line medicaments for controlling blood pressure.

Accordingly, each and every element of the new claims is found in the specification as originally filed.

Replacement page:

As provided in the Rules, a replacement page that includes new claims 44 and 45 is attached hereto. Also attached is a page with the new claims with markings showing the new claims. Claims 1 – 43 have not been amended and are unchanged from the original filing.

Very truly yours,



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Enclosures

independently substituted or unsubstituted, which if substituted, are substituted with one or more substituents selected from R^{11};

R^6 and R^{10} are independently selected from -H and alkyl;

R^7 and R^8 are independently selected from -H, alkyl, alkenyl, alkynyl, -$CONR^5R^9$, alkyl-$CONR^5R^9$, alkylthio-R^{10}, thioalkyl, aminoalkyl, alkylamino-R^{10}, cycloalkyl, aryl, aralkyl, wherein R^7 and R^8 are independently substituted or unsubstituted, which if substituted, are substituted with one or more substituents selected from R^{11};

R^{11} is selected from halo and haloalkyl;

X^1 is optionally present, and if present, is alkyl; and

including the isomers, racemates, salts, and prodrugs thereof.

41. The method according to claim 40, wherein the β-adrenergic agonist comprises a β_2-adrenergic agonist.

42. The method according to claim 41, wherein the β_2-adrenergic agonist comprises at least one compound chosen from metaproterenol, pirbuterol, albuterol, levalbuterol, formoterol, salmeterol, terbutaline, isoetharine, levalbuterol, salbutamol, bambuterol, fenoterol, reproterol, tulobuterol, and mixtures thereof.

43. Use of a compound having a structure described in claim 22 alone or in combination with a β-adrenergic agonist for the production of a medicament for the preventing or treating a cardiovascular or respiratory disorder in a subject.

44. (New) A method of preventing or treating a cardiovascular or respiratory disorder in a subject, the method comprising administering to the subject an effective amount of a compound having a structure described in claim 1 in combination with a conventional treatment agent.

45. (New) The method according to claim 44, wherein the conventional treatment agent is a calcium channel blocker.

independently substituted or unsubstituted, which if substituted, are substituted with one or more substituents selected from R^{11};

R^6 and R^{10} are independently selected from -H and alkyl;

R^7 and R^8 are independently selected from -H, alkyl, alkenyl, alkynyl, -$CONR^5R^9$, alkyl-$CONR^5R^9$, alkylthio-R^{10}, thioalkyl, aminoalkyl, alkylamino-R^{10}, cycloalkyl, aryl, aralkyl, wherein R^7 and R^8 are independently substituted or unsubstituted, which if substituted, are substituted with one or more substituents selected from R^{11};

R^{11} is selected from halo and haloalkyl;

X^1 is optionally present, and if present, is alkyl; and

including the isomers, racemates, salts, and prodrugs thereof.

41. The method according to claim 40, wherein the β-adrenergic agonist comprises a β_2-adrenergic agonist.

42. The method according to claim 41, wherein the β_2-adrenergic agonist comprises at least one compound chosen from metaproterenol, pirbuterol, albuterol, levalbuterol, formoterol, salmeterol, terbutaline, isoetharine, levalbuterol, salbutamol, bambuterol, fenoterol, reproterol, tulobuterol, and mixtures thereof.

43. Use of a compound having a structure described in claim 22 alone or in combination with a β-adrenergic agonist for the production of a medicament for the preventing or treating a cardiovascular or respiratory disorder in a subject.

44. A method of preventing or treating a cardiovascular or respiratory disorder in a subject, the method comprising administering to the subject an effective amount of a compound having a structure described in claim 1 in combination with a conventional treatment agent.

45. The method according to claim 44, wherein the conventional treatment agent is a calcium channel blocker.

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IAP20 Rec'd PCT/PTO 10 MAY 2006

TRANSMITTAL LETTER TO THE UNITED STATES RECEIVING OFFICE

Express Mail mailing number: VIA FAX 011-41-22-740-14-35	Date of deposit: Transmitted 4/27/05
File reference no.: 16139/09052-PCT	International application no. (if known): PCT/US04/037813
Title of the invention: TREATMENT OR PREVENTION OF CARDIOVASCULAR AND RESPIRATORY DISORDERS WITH NOVEL SUBSTITUTED CYCLIC AMP-SPECIFIED PHOSPHODIESTERASE INHIBITORS	
Earliest priority date claimed (Day/Month/Year): 12 November 2003 (12.11.03)	

☐ **This is a new International Application**

SCREENING DISCLOSURE INFORMATION:

In order to assist in screening the accompanying international application for purposes of determining whether a license for foreign transmittal should and could be granted and for other purposes, the following information is supplied. (check as many boxes as apply):

☐ The invention disclosed was **not** made in the United States of America.

☐ There is no prior U.S. application relating to this invention.

☐ The following prior U.S. application(s) contain subject matter which is related to the invention disclosed in the attached international application. *(NOTE: priority to these applications may or may not be claimed on the Request (form PCT/RO/101) and this listing does **not** constitute a claim for priority.)*

application no.		filed on	
application no.		filed on	

☐ The present international application contains additional subject matter not found in the prior U.S. application(s) identified above. The additional subject matter is found on pages _____ and ☐ **DOES NOT ALTER** ☐ **MIGHT BE CONSIDERED TO ALTER** the general nature of the invention in a manner which would require the U.S. application to have been made available for inspection by the appropriate defense agencies under 35 U.S.C. 181 and 37 C.F.R. 5.15.

Itemized list of contents

Sheets of Request form:	Check no.:
Sheets of description (excluding sequence listing):	Return receipt postcard:
Sheets of claims:	Power of attorney:
Sheets of abstract:	Certified copy of priority document (specify):
Sheets of drawings:	Other (specify): Certificate of Facsimile Transmission (1 page); Letter (2 pages) with replacement pages (2 pages).
Sheets of sequence listing:	
Sequence listing diskette/CD:	
Tables related to sequence listing CD:	

The person signing this form is:

☐ Applicant

☑ Attorney/Agent (Reg. No.)

☐ Common Representative

Charles E. Dunlap, Esq.
Registration No. 35,124
Name of person signing

Signature

This collection of information is required by 37 CFR 1.10 and 1.412. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**